

Amendments to the Specification:**BEST AVAILABLE COPY**

On page 1, starting on line 27 and ending on line 34, please replace the paragraph with the following amended paragraph:

This application is a continuation of and claims priority under 35 U.S.C. § 120 to co-pending application number, 10/695,582, filed October 28, 2003, which is a continuation of co-pending application, 10/431,467, filed May 7, 2003, which is a continuation of co-pending application 10/374,805, filed February 25, 2003, which is a continuation of co-pending application number 10/058,695, filed January 28, 2002, which is a continuation of co-pending application 10/004,571, filed December 4, 2001, which is a continuation of co-pending application 09/874,514, filed June 5, 2001, which is a continuation of co-pending application 09/808,451, filed March 31, 2001, now U.S. Patent 6,656,961, issued December 2, 2003, which is a continuation of co-pending application 09/686,158, filed October 11, 2000, now U.S. Patent 6,369,234, issued April 9, 2002, which is a continuation of co-pending application 09/662,426, filed September 13, 2000, now U.S. Patent 6,300,355, issued September 13, 2000, which is a continuation of co-pending application 09/691,615, filed October 18, 2000, now U.S. Patent 6,284,781, issued September 4, 2001, which is a continuation of application 08/986,025, filed December 3, 1997, now U.S. Patent 6,242,469, issued June 5, 2001, which claims priority under 35 U.S.C. § 119(e) to [is based on] U.S. Provisional Application Serial Nos. 60/032,282, 60/033,767, 60/047,566, 60/047,941, and 60/055,533, filed December 3, 1996, January 14, 1997, May 22, 1997, May 29, 1997, and August 13, 1997, respectively, the contents of which are hereby incorporated by reference into this application. This invention was made with government support under grants CA-28824, CA-39821, CA-GM 72231, CA-62948, and AI0-9355 from the National Institutes of Health, and grant CHE-9504805 from the National Science Foundation. Additionally, the present invention was supported in part by a fellowship from the United States Army to Dongfang Meng (DAMD 17-97-1-7146), and thus the government has certain rights in the invention.

On page 3, lines 21-22, please replace the paragraph with the following amended paragraph:

[Figure 3A provides] Figures 3(A) and 3(B) provide syntheses of key iodinated

BEST AVAILABLE COPY

intermediates used to prepare hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives..

On page 3, lines 24-27, please replace the paragraph with the following amended paragraph:

[Figure 3B provides] Figures 3(C) and 3(D) provide methods of preparing hydroxymethylene- and hydroxypropylene-substituted epothilone derivatives, said methods being useful generally to prepare 12,13-*E* epothilones wherein R is methyl, ethyl, n-propyl, and n-hexyl from the corresponding *E*-vinyl iodides.

On page 3, lines 29-30, please replace the paragraph with the following amended paragraph:

[Figure 3B shows] Figures 3(E) and 3(F) show reactions leading to benzoylated hydroxymethyl-substituted desoxyepothilone and hydroxymethylene-substituted epothilone (epoxide).

On page 4, line 9, please replace the paragraph with the following amended paragraph:

[Figure 6 provides] Figures 6(A) and 6(B) provide a scheme of an olefin metathesis route to epothilone A and other analogues.

On page 4, line 29, please replace the paragraph with the following amended paragraph:

[Figure 14 shows] Figures 14(A) and 14(B) show the preparation of intermediate 4A.

On page 5, lines 7-8, please replace the paragraph with the following amended paragraph:

[Figure 18 provides] Figures 18(A) and 18(B) provide a synthetic pathway to a protected intermediate for 8-desmethyl deoxyepothilone A

On page 5, lines 10-11, please replace the paragraph with the following amended

Page 3 of 14

BEST AVAILABLE COPY

paragraph:

[Figure 19 provides] Figures 19(A), 19(B) and 19(C) provide a synthetic pathway to 8-desmethyl deoxyepothilone A, and structures of *trans*-8-desmethyl-desoxyepothiolone A and a *trans*-iodoolefin intermediate thereto.

On page 5, lines 13-22, please replace the paragraph with the following amended paragraph:

[Figure 20 shows (top)] Figure 20(A) shows structures of epothilones A and B and 8-desmethylepothilone and [bottom] Figure 20(B) shows a synthetic pathway to intermediate TBS ester 10 used in the preparation of desmethylepothilone A. (a) (Z)-Crotyl-B[(-)-Ipc]₂, -78°C, Et₂O, then 3N NaOH, 30% H₂O₂; (b) TBSOTf, 2,6-lutidine, CH₂Cl₂ (74% for two steps, 87% ee); (c) O₃, CH₂Cl₂/MeOH, -78°C, then DMS, (82%); (d) *t*-butyl isobutyrylacetate, NaH, BuLi, 0°C, then 6 (60%, 10:1); (e) Me₄NBH(OAc)₃, -10°C (50%, 10:1 α/β) or NaBH₄, MeOH, THF, 0°C, (88%, 1:1 α/β); (f) TBSOTf, 2,6-lutidine, -40°C, (88%); (g) Dess-Martin periodinane, (90%); (h) Pd(OH)₂, H₂, EtOH (96%); (i) DMSO, oxalyl chloride, CH₂Cl₂, -78°C (78%); (j) Methyl triphenylphosphonium bromide, NaHMDS, THF, 0°C (85%); (k) TBSOTf, 2,6-lutidine, CH₂Cl₂, rt (87%).

On page 5, line 29, please replace the paragraph with the following amended paragraph:

[Figure 22 shows] Figures 22(A), 22(B) and 22(C) show a synthetic pathway to prepare epothilone analogue 27D.

On page 5, line 31, please replace the paragraph with the following amended paragraph:

[Figure 23 shows] Figures 23(A), 23(B) and 23(C) show a synthetic pathway to prepare epothilone analogue 24D.

BEST AVAILABLE COPY

On page 5, line 33, please replace the paragraph with the following amended paragraph:

[Figure 24 shows] Figures 24(A) and 24(B) show a synthetic pathway to prepare epothilone analogue 19D.

On page 5, line 35, please replace the paragraph with the following amended paragraph:

[Figure 25 shows] Figures 25(A), 25(B), 25(C) and 25(D) show a synthetic pathway to prepare epothilone analogue 20D.

On page 5, line 37, please replace the paragraph with the following amended paragraph:

[Figure 26 shows] Figures 26(A), 26(B), 26(C) and 26(D) show a synthetic pathway to prepare epothilone analogue 22D.

On page 6, lines 1-2, please replace the paragraph with the following amended paragraph:

[Figure 27 shows] Figures 27(A), 27(B) and 27(C) show a synthetic pathway to prepare epothilone analogue 12-hydroxy ethyl-epothilone.

On page 6, lines 4-7, please replace the paragraph with the following amended paragraph:

[Figure 28 shows] Figures 28(A) and 28(B) show the activity of epothilone analogues in a sedimentation test in comparison with DMSO, epothilone A and/or B. Structures 17-20, 22, and 24-27 are shown in Figures 29-37, respectively. Compounds were added to tubulin (1mg/ml) to a concentration of 10 μ M. The quantity of microtubules formed with epothilone A was defined as 100%

On page 6, lines 30-32, please replace the paragraph with the following amended paragraph:

BEST AVAILABLE COPY

[Figure 39 shows] Figures 39(A) and 39(B) show epothilone A and epothilone analogues #1-7. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

On page 6, lines 34-36, please replace the paragraph with the following amended paragraph:

[Figure 40 shows] Figures 40(A) and 40(B) show epothilone B and epothilone analogues #8-16. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

On page 7, lines 1-3, please replace the paragraph with the following amended paragraph:

[Figure 41 shows] Figures 41(A) and 41(B) show epothilone analogues #17-25. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

On page 7, lines 5-7, please replace the paragraph with the following amended paragraph:

[Figure 42(A) shows] Figures 42(A) and 42(B) show epothilone analogues #26-34. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

On page 7, lines 10-12, please replace the paragraph with the following amended paragraph:

[Figure 42(B) shows] Figures 42(C) and 42(D) show epothilone analogues #35-46. Potencies against human leukemia CCRF-CEM (sensitive) and CCRF-CEM/VBL MDR (resistant) sublines are shown in round and square brackets, respectively.

On page 7, line 14, please replace the paragraph with the following amended paragraph:

[Figure 42(C) shows] Figure 42(E) shows epothilone analogues #47-49.

Page 6 of 14

THIS PAGE LEFT BLANK